

## Vaccines as instruments of foreign policy

The new vaccines for tropical infectious diseases may have unanticipated uses beyond fighting diseases • *by Peter J. Hotez*

Nearly a century ago, in 1913, the International Health Board of the Rockefeller Foundation in New York City almost single-handedly created American tropical medicine research. Through a focused programme of philanthropic support for research on the treatment and prevention of infections such as malaria, yellow fever and hookworm, they initiated efforts to fight those diseases that affect the world's poorest nations. Simultaneous funding for The Rockefeller Institute for Medical Research, new institutions of public health at Johns Hopkins and Harvard University, and overseas research and educational institutions in Brazil and China further created an infrastructure by which American tropical disease research and development was supported and sustained.

The development of the yellow fever vaccine and the eradication of malaria in many parts of the world are among the many achievements that resulted from the Rockefeller initiative. But the last two decades have witnessed a decrease in clinical and laboratory tropical disease research. During this period, the Rockefeller Foundation gradually moved away from funding biomedical research and left this task to organisations without experience in tropical disease research, such as the MacArthur Foundation. Unfortunately, these foundations were not prepared or committed to support work in this difficult field in the long term. Moreover, both the Tropical Disease Research programme of the World Health Organization (WHO) and the international programmes of the US National Institutes of Health (NIH) suffered from chronic under-funding. Thus, during the late 1980s and early 1990s, American scientists began leaving research on tropical diseases at an alarming rate. This scientific exodus occurred at a time when 2 million children were dying each year from

malaria, when children's hospital wards in Southeast Asia and Central America regularly filled with cases of dengue haemorrhagic fever, and when soil-transmitted helminthiases were the most prevalent infections on Earth. The dwindling resources for developing world health in

Sierra Leone became the 'poster children' for this new world order. This period also heralded a resurgence in funding for the treatment and prevention of tropical diseases.

Indeed, the new millennium is the harbinger of a renaissance in tropical disease

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**The dwindling resources for developing world health in the context of a booming stock market and economic growth and prosperity threatened to tarnish the 1990s as a decade of moral outrage**

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the context of a booming stock market and unprecedented economic growth and prosperity in the USA threatened to tarnish the 1990s as a decade of moral outrage. Former Secretary of State Henry Kissinger labels this period as a paradox:

'On the one hand, the United States is sufficiently powerful to be able to insist on its view and to carry the day often enough to evoke charges of American hegemony. At the same time, American prescriptions for the rest of the world often reflect either domestic pressures or a reiteration of maxims drawn from the experience of the Cold War. The result is that the country's preeminence is coupled with the serious potential of becoming irrelevant to many of the currents affecting and ultimately transforming the global order [...] At the apogee of its power, the United States finds itself in an ironic position. In the face of perhaps the most profound and widespread upheavals the world has ever seen, it has failed to develop concepts relevant to the emerging realities.' (Kissinger, 2001).

The concept of 'universal humanitarian intervention' finally took hold in the second half of the 1990s (Kissinger, 2001) when military operations by the United States, Western Europe and Australia in Haiti, Somalia, Kosovo, East Timor and

research that resembles the Rockefeller philanthropy at the turn of the last century. In an extraordinary two-year burst of activity, vast amounts of new private and federal funds were infused into what the late Kenneth Warren of the Rockefeller Foundation often referred to as 'the great neglected diseases of mankind'. Funds from the Bill and Melinda Gates Foundation

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([www.gatesfoundation.org](http://www.gatesfoundation.org)) and Ted Turner received the greatest attention, but the National Institute of Allergy and Infectious Diseases (NIAID) of the NIH and nascent foundations like the Burroughs Wellcome Fund and Ellison Medical Foundation are also helping to revive a moribund US tropical disease research effort. The Rockefeller Foundation also renewed their commitment to funding biomedical research through financing the International AIDS vaccine initiative.

**Table I.** New vaccine initiatives for developing countries

Vaccine initiative	Recipient	Location	Amount of funding
<b>New Vaccine Initiatives funded by the Bill &amp; Melinda Gates Foundation</b>			
Children's vaccine Fund	GAVI	Geneva	\$ 750 million
International AIDS vaccine initiative	IAVI	New York	\$ 125 million
Meningitis vaccine project	PATH-WHO	Geneva	\$ 70 million
Malaria vaccine initiative	PATH	Washington, DC	\$ 50 million
Cholera/Typhoid/ <i>Shigella</i> vaccines	IVI	Seoul	\$ 40 million
Tuberculosis vaccine initiative	Sequella	Washington, DC	\$ 25 million
Improved measles vaccine initiative	University of Maryland	Baltimore	\$ 20 million
Improved measles vaccine initiative	Johns Hopkins University	Baltimore	\$ 20 million
Human hookworm vaccine initiative	Sabin Institute/GW	Washington, DC	\$ 18 million
Leishmaniasis vaccine initiative	IDRI/Corixa	Seattle	\$ 15 million
<b>Related Gates Foundation Initiatives to Combat Tropical Infectious Diseases</b>			
MDR Tuberculosis control	Harvard	Boston	\$ 45 million
Malaria treatment & prevention	London SHTM	London	\$ 40 million
Drug & vaccine supply program	MSH	Boston	\$ 30 million
International trachoma initiative	ITI	Geneva/NY	\$ 20 million
Lymphatic filariasis elimination	World Bank	Washington, DC	\$ 20 million
Drugs for African Sleeping Sickness	University of NC	Chapel Hill	\$ 15 million
Tuberculosis diagnostic initiative	TDR/WHO	Geneva	\$ 10 million
<b>New Vaccine Initiatives funded by NIAID, NIH</b>			
Malaria vaccine initiative	SAIC	Washington, DC	\$ 40 million
NIAID Global Health Research Plan	NIAID, NIH	Washington, DC	

Sources: [www.gatesfoundation.org](http://www.gatesfoundation.org) and [www.niaid.nih.gov](http://www.niaid.nih.gov).

As shown in Table I, the funding is targeted to new or improved vaccines for the great scourges of the tropics such as malaria, HIV/AIDS, tuberculosis, measles, meningococcal meningitis, enteric bacteria, hookworm and leishmaniasis. Overall, funds will exceed US\$ 1 billion and an almost equal amount has been set aside to improve the delivery of existing vaccines. Here, the magnitude of the Gates funding for vaccine R&D dwarfs all previous funding from the Rockefeller Foundation,

**The new vaccines for tropical diseases will surpass the sophistication—and the costs—of existing ones by an order of magnitude or more**

WHO or any single national government.

The new vaccines for tropical infectious diseases require such a high level of financial support because they will be

expensive to develop, produce and test. The previous generation of vaccines for infections such as polio and measles relied on relatively cheap *in vitro* culture technology. But for many tropical diseases, exposure to or experience of the infectious agent does not confer immunity. Therefore, unlike vaccines for polio or measles, new vaccines must elicit immune responses that may not ordinarily occur in nature. New platform technologies, novel expression vectors, and a new generation of adjuvants are needed in order to induce protective immunity. It is almost certain that such vaccines will surpass both the sophistication—and the costs—of existing vaccines by an order of magnitude or more. And the most expensive and complex vaccines are being targeted at the most destitute who live in countries whose governments are least able to accommodate either the costs or the complexity.

Bridging the gap between the biomedical and social sciences as they pertain to developing countries is, therefore, one of the greatest challenges that could otherwise thwart the introduction of new vaccines. The endgame is no longer simply how to make the best vaccine in the laboratory, but rather how vaccines will be purchased and used appropriately. Through new institutions such as the Glo-

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bal Alliance for Vaccines and Immunizations (GAVI), in partnership with WHO and non-governmental organisations, an unprecedented dialogue among vaccine scientists, social scientists and industrialists is beginning to take place concerning

how the new vaccines will be financed and who will pay the bills. To begin to chip away at this problem, economists from Harvard and Yale University, The Brookings Institution and The World Bank are taking crash courses in tropical disease prevention and a recent conference held at Cold Spring Harbor Laboratory generated an impressive range of global vaccine financing schemes (Muraskin, 2001). These will converge into a broader and more comprehensive world-wide health fund first proposed at the G8 summit in Okinawa in 2000 and now taking shape through the UN General Assembly. But the vaccine financing schemes emerging from these interdisciplinary forays will require considerable refinement. Many of the suggested programmes lack reality testing and require greater input from the four major global vaccine manufacturers. However, innovative solutions are being generated and serviceable international vaccine financing initiatives will be forthcoming.

Economists are not the only social scientists who will be called upon to address the complexities of the new vaccines in the era of globalisation. Sociologists and anthropologists could be tapped to help vaccinologists identify populations who might benefit the most from the new vaccines. For instance, some vaccines could target young women of child-bearing age or specific age groups other than infants and toddlers who traditionally receive their vaccines under WHO's Expanded Program on Immunisation. Finally, the study of political science will be brought into the fold in order to explore the role of vaccines in conducting diplomacy and foreign policy.

Indeed, the notion that vaccines may function as agents of conflict resolution is one that has deep historical roots (Hotez, 2001). Edward Jenner, the British inventor of the first smallpox vaccine, was considered a hero in France as well as in England and was called upon to mediate prisoner exchanges. Jenner was elected as a foreign member of the Institute of France at a time of almost continuous warfare between the two nations during the early 1800s (Bazin, 2000).

The modern era of American vaccine diplomacy followed on the heels of the Marshall Plan when US technical and scientific resources were first engaged in foreign policy. In the 1950s, when polio epidemics occurred every summer in

North America, Europe and the USSR, Albert Sabin began to work closely with Soviet virologists in order to develop, test and license the live polio vaccine. It is not widely known that the attenuated polio strains developed in Sabin's laboratory at the University of Cincinnati were transformed into a clinically useful oral

## The notion that vaccines may function as agents of conflict resolution is not new

vaccine with the help of Soviet virologists. Presumably it was the terror that polio inflicted into parents on both sides of the Atlantic that prompted both the Americans and Soviets to set aside their ideological differences in 1956 (Benison, 1982). At the height of the Cold War, leading Soviet virologists travelled to Cincinnati where they obtained a commitment from Dr Sabin to provide them with his vaccine strains. In a landmark reciprocal visit a few months later, Sabin received permission to visit the laboratories of Soviet scientists. Both exchanges proceeded with the tacit approval of a stridently anti-communist Republican Eisenhower administration. What followed was a remarkable example of Cold War diplomacy, in which Soviet children were among the first to receive test doses of the oral polio vaccine. By 1960, millions of Soviet children were vaccinated. Only after its safety had been established in the USSR and validated by Dorothy Horstmann from Yale, was the Sabin vaccine approved and licensed in the USA. Similar co-operation channelled through the WHO led to the introduction of essential smallpox freeze-drying technology (Fenner, 1996). Like polio, the control and ultimately the eradication of smallpox was the product of Cold War vaccine diplomacy.

The successful American–Soviet bilateral co-operation that spearheaded the wars on polio and smallpox certainly made a deep impression on the two Democratic administrations in the White House during the early and mid-1960s. President Kennedy sent an estimated \$35 million worth of medicines and medical supplies to Cuba in exchange for assurances from Fidel Castro to release 1700 prisoners following the Bay of Pigs debacle (Carey, 1970). The creation of the US

Agency for International Development and the Peace Corps during the Kennedy administration possibly had its roots in the Cold War successes attributed to vaccine diplomacy. In 1966, President Johnson undertook an ambitious, albeit ultimately futile, effort to institutionalise vaccine diplomacy. The International Health Education Act called for an expenditure of \$10 million for overseas health and health education because as the then Secretary of Health, Education, and Welfare John Gardner put it, 'There are no better grounds on which we can meet other nations and demonstrate our own concern for peace and the betterment of mankind than in a common battle against disease' (Carey, 1970). Despite vigorous lobbying by the Johnson administration, the legislation died in the House Rules Committee (Carey, 1970). Since then, medical interventions have not been a cornerstone of American foreign diplomacy.

Outside the United States vaccine diplomacy has remained active through the efforts of UNICEF (Hotez, 2001). Since 1994, UNICEF, as well as other NGOs have successfully negotiated cease-fires during civil conflicts through vaccination campaigns against polio as well as annual 'days of tranquility' held in Afghanistan ([www.unicef.org](http://www.unicef.org)). National immunisation days have also temporarily halted hostilities in some of the most intractable African civil conflicts in Sudan, Sierra Leone and the Democratic Republic of Congo (Table II).

It remains to be seen whether the vaccine initiatives that brokered Cold War diplomacy in the 1950s and 1960s or the polio immunisations used to mediate civil conflicts in the 1990s might also be

**Table II.** UNICEF vaccine-mediated cease-fires during civil conflicts

Date	Location
June 1996	Liberia
July 1998	Sudan
June 1999	Afghanistan
May 2000	Afghanistan
August 2000	DR Congo
October 2000	Afghanistan
October 2000	Sudan

Sources: [www.unicef.org](http://www.unicef.org) and [www.bbc.co.uk](http://www.bbc.co.uk).

leveraged into a more permanent component of US foreign policy. Increasing attention has been given to the concept that tropical infectious diseases destabilise communities and thereby threaten domestic and even international security (www.crisisweb.org). The HIV/AIDS epidemic, for example, is creating millions of orphans in parts of sub-Saharan Africa, who might one day comprise a new generation of militias and armies.

Analysis suggests that a possible relationship may exist between childhood death rates from vaccine-preventable infections and the probability of a nation becoming engaged in armed conflict. Most of the leading killers of children under the age of five are infectious agents endemic to developing countries (Murray and Lopez, 1996; WHO and UNICEF, 1996), with the measles virus and the malaria parasite *Plasmodium falciparum* heading the list (Table III). Perhaps the most remarkable feature about these infections is that at least six of them—measles, rotavirus diarrhoea, pneumococcal and Haemophilus influenzae type b meningitis, tetanus and pertussis—can be largely prevented through use of safe, inexpensive and available vaccines.

The fact that more than 5 million children still die needlessly because they do not receive their vaccinations is one of the great tragedies of the new

millennium. Yet there are implications that extend beyond the appalling death toll. The childhood mortality figures paired with listings of major conflicts between the years 1990 and 2000 suggest

No evidence is currently available to suggest that aggressive vaccination together with its expected decrease in childhood mortality would pre-empt an armed conflict. However, given its

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a strong positive correlation between the two. As shown in Figure 1, 12 of the 18 countries with infant mortality rates greater than 110 deaths per 1000 were engaged in an armed conflict between 1990 and 2001, whereas no nations with low infant mortality rates were at war during this time. The correlation between childhood mortality under the age of five—predominantly from infectious diseases—and waging war is particularly striking (Figure 2), as the percentage of countries at war sharply increases whenever childhood mortality rates exceed 100 deaths per 1000. These data can be used to derive a theoretical probability for becoming engaged in armed conflict. Nations such as Afghanistan and Sierra Leone with child mortality rates that exceed 150 deaths per 1000 are 17.5 times more likely to be engaged in hostilities compared with countries such as Denmark or the USA (Table IV).

immediate benefit, it would be of interest to examine the long-term impact of childhood vaccination on a nation's foreign policy.

The developing economies of Asia offer attractive targets for implementing vaccine diplomacy. Nation states in both East and Central Asia are noted for their high rates of infectious diseases and yet they also benefit from advanced infrastructures that are capable of conducting complex diplomatic missions. Some Asian countries also nurture sophisticated biomedical research institutes with capacity for vaccine R&D and distribution. Three potential regions for vaccine diplomacy include Korea, the new Shanghai Cooperation Organisation (SCO) alliance, and South Asia.

In its new dialogue with North Korea, The Bush Administration might consider the potential for vaccine R&D and distribution in order to achieve its

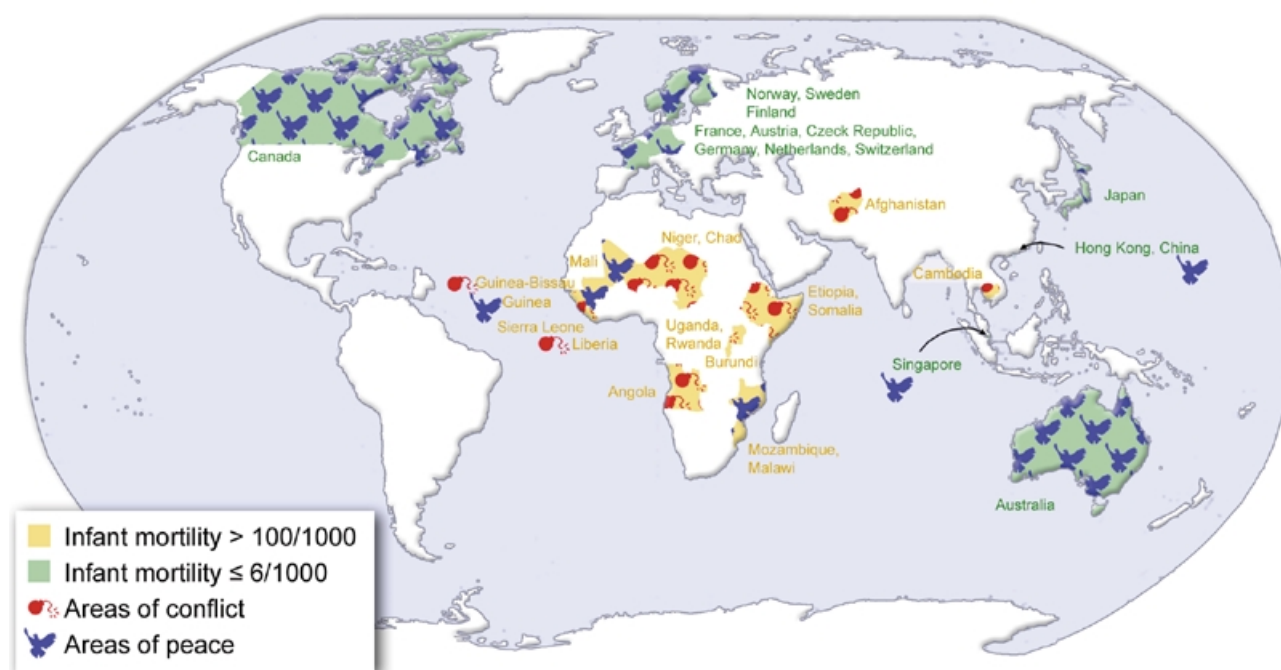
**Table III.** The 10 leading childhood killers (< 5 years old) and childhood disablers (5–14 years old)

The 10 leading childhood killers <sup>a</sup>		The nine leading childhood disablers <sup>b</sup>		
Number of annual deaths (< 5 years old)		Disability adjusted life years × 1000 (5–14 years old)		
		Male	Female	
Measles	>1 million			
<i>Falciparum</i> malaria	>1 million	injuries	47 323	30 236
Pneumococcus	0.9 million	pneumonia	9327	10 773
RSV	0.9 million	diarrheal disease	6191	6934
Rotavirus	0.9 million	measles	5252	5298
<i>Shigella</i> (dysentery)	0.6 million	malaria	3458	3495
Haemophilus type B	0.5 million	geohelminths	2891	2850
Tetanus (neonatal)	0.5 million	iron deficiency	2468	2470
Pertussis	0.4 million	tuberculosis	2005	2346
Tuberculosis	0.3 million	war	2365	1791

<sup>a</sup>Source: WHO and UNICEF (1996).

<sup>b</sup>Source: Murray and Lopez (1996).





**Fig. 1.** Relationship between infant mortality rates and armed conflict. Data from the Carnegie Commission on Preventing Deadly Conflict (1997); Smith (1997); UN Population Fund (1999).

diplomatic goals. The Democratic People's Republic of Korea is emerging from a devastating famine, with up to 3 million deaths attributed to starvation. Widespread malnutrition together with a breakdown in public health infrastructure creates conditions that permit microbial pathogens to re-emerge and flourish. There has already been a

resurgence of polio, tuberculosis and malaria ([www.who.int](http://www.who.int)), and the nation's infant mortality is now one of the highest in Asia. In collaboration with the International Vaccine Institute located on the campus of Seoul National University ([www.ivi.org](http://www.ivi.org)), a sister institution could be established in the North, where it also might help to

redirect North Korea's bioweapons production capabilities ([www.fas.org/nuke/guide](http://www.fas.org/nuke/guide)).

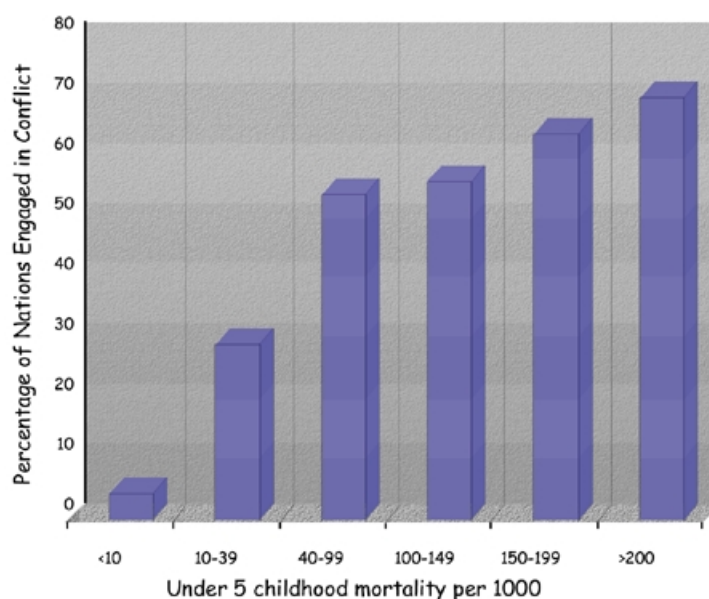
Previously known as the 'Shanghai Five', the nations of China, Kazakhstan, Kyrgyzstan, Russia and Tajikistan have established the SCO in order to both reduce tensions along the Sino-Russian border and halt the spread of separatist

**Table IV.** Probability of being involved in an armed conflict based on under 5-year childhood mortality rates

Childhood mortality rate	Number of nations	Percentage in conflict	Risk
Less than 10 per 1000	26	4%	—
10–39 per 1000	52	29%	7.2
40–99 per 1000	26	54%	13.5
100–149 per 1000	25	56%	14
150–199 per 1000	11	64%	16
Greater than 200 per 1000	10	70%	17.5

Childhood mortality rates were based on the 1998 World Development Indicators ([www.worldbankgroup.org](http://www.worldbankgroup.org)), except for Afghanistan, Bosnia and Herzegovina, Denmark, Djibouti, Gambia, Laos, Liberia, Somalia and the United States for which no data were reported. For these countries I relied on 1996 data from McDevitt, cited in [www.overpopulation.com](http://www.overpopulation.com).

The nations engaged in armed conflict were identified by the Carnegie Commission to Prevent Conflict (1997). The nations of Djibouti, Egypt, Ethiopia, Libya, Mauritania, Myanmar (Burma), Niger, Papua New Guinea, Philippines, Senegal and Togo were not identified as countries in conflict on this list, although they were identified as countries in armed conflict by Smith (1997). Cote d'Ivoire and Macedonia were added to the list of nations in conflict following the 1997 publication date of both references.



**Fig. 2.** Relationship between under 5-year childhood mortality (per 1000) and Armed Conflict during the 1990s. Source data: [www.worldbankgroup.org](http://www.worldbankgroup.org), [www.overpopulation.com](http://www.overpopulation.com), Smith (1997) and Carnegie Commission on Preventing Deadly Conflict (1997).

movements in the region (Ni, 2001). The alliance could solidify and strengthen their union through vaccine diplomacy. Infectious pathogens may pose as great a threat to the national security of the SCO alliance member nations as rebel insurgencies, or even NATO's proposed missile defence system. For instance, the number of annual deaths from tuberculosis may exceed 1.5 million in Russia, and multi-drug resistant *Mycobacterium tuberculosis* (MDR TB) may move into Northern Europe and Central Asia. Vaccines to combat MDR TB offer a chance for the SCO to work together in fighting their greatest enemy. The SCO has already formed a joint anti-terrorism centre in Bishkek, the capital of Kyrgyzstan. Assistance could be offered to establish a research centre in Bishkek devoted to MDR TB. SCO vaccine initiatives could also help redirect the vast former Soviet bioweapons industry into peacetime vaccine R&D (Geissler and Woodall, 1994).

The possibility that India and Pakistan might be added to the list of SCO member states also presents an opportunity for vaccine R&D collaboration. Together with China, these three nations comprise approximately 40% of the world's population. International border conflicts are a

dominant theme in the modern history of this region, including a Sino-Indian war in 1962, as well as recent clashes over disputed areas of Kashmir. The hostilities have constituted a stimulus for renewed nuclear weapons testing by India and Pakistan within the last three years. Possibly more than anywhere else, South Asia has the highest likelihood of becoming engaged in a nuclear conflict. Ironically, these technologically sophisticated countries also share the highest rates of endemic tropical infectious diseases—malaria, TB, HIV/AIDS, soil transmitted helminthiases—including many that will be targeted by the new vaccines (Hotez *et al.*, 1997; Hotez, 2001). A multilateral programme focused on disease might foster regional co-operation and promote peace and stability. The control of infectious pathogens could replace atomic weapons as a source of national pride in South Asia.

History indicates that vaccines were powerful instruments of foreign policy in the 20<sup>th</sup> Century. The new philanthropy to develop tropical disease vaccines will ensure development of an extraordinary product line for combating some the Earth's greatest plagues. The new vaccines will continue to expand the legacy of vaccine diplomacy—an

emerging foreign policy theme for the 21<sup>st</sup> century.

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## ‘How can we know the dancer from the dance?’—William B. Yeats

To solve problems in the new millennium, society needs more, not less science  
• by David McConnell

The natural sciences have often been regarded with concern and suspicion in the non-scientific world. This is by no means a new phenomenon. Galileo faced criticism for his statement that the Earth revolved around the Sun. Charles Darwin's *The Origin of Species* stirred up heavy criticisms from those who believed in a divine creation of man. Today, due to the larger influence of science on society, this problem is even greater, particularly regarding the extraordinary discoveries in the field of genetics. Society's disquiet about science is damaging to science itself and reduces the social, economic

In November 2000, I participated in the ‘Genetics and the Future of Europe’ conference, organised by Commissioner

accept that they and science should take most of the blame for many different problems, which, it is alleged, are caused by

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Busquin in Brussels. It was a valuable initiative, an attempt to start a public dialogue between life scientists and representatives of ‘society’. But instead of being elated and joyful about their

science. Moreover, there was a reluctance to turn the argument in the other direction, to speak more of the beauty of scientific knowledge rather than the horror, the value rather than the cost and the importance for society rather than the risk. Of course, there are faults within science, but I think we need to be clear that the main weaknesses relating to science lie in the general, non-scientific body politic. This is not a matter of apportioning blame, but rather of defining where the problems lie. The simple fact is that society requires a deeper understanding of science.

**Society's disquiet about science is damaging to science itself and reduces the social, economic and cultural value of research**

and cultural value of research. It has thus become necessary to find means to bring the natural sciences and the humanities together in order to overcome society's fears.

science, some of my colleagues appeared to have been wounded by the barrage of criticism. Indeed, I sensed a defensiveness among scientists who seemed ready to